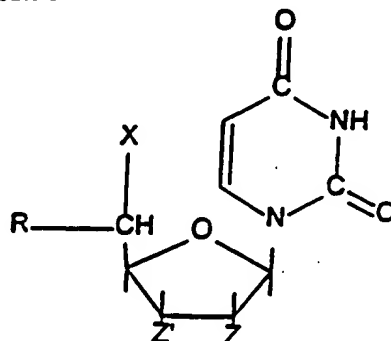


## WE CLAIM:

1. A combinatorial library comprising a predetermined collection of nucleoside peptide molecules for inhibiting the transfer of a sugar from a selected sugar nucleotide donor to a selected acceptor by a carbohydrate processing enzyme wherein a nucleoside peptide molecule comprises (a) a nucleoside monomer; (b) a spacer monomer coupled to the nucleoside monomer wherein the spacer monomer comprises one or more amide linked amino acid residues or mimetics thereof; and (c) cap monomers attached to the spacer monomer; wherein the nucleoside peptide molecules differ from each other as to the identity of at least one element of the nucleoside monomer, spacer monomer or cap monomers.
2. A combinatorial library as claimed in claim 1 wherein the carbohydrate processing enzyme is a glycosyltransferase involved in the biosynthesis of glycoproteins, glycolipids, or glycosyl phosphatidyl inositols.
3. A combinatorial library as claimed in claim 2 wherein the carbohydrate processing enzyme is an N-acetylglucosaminyltransferase I, II, III, IV, or V, or  $\beta$ -1,3-galactosyl-O-glycosyl-glycoprotein  $\beta$  1,6-N-acetylglucosaminyl transferase (core 2 GlcNAc).
4. A combinatorial library as claimed in claim 1, 2, or 3 wherein the nucleoside monomer is uridyl, 2'-deoxyuridyl, or 5'-amino-5'-deoxy-2',3'-O-isopropylidene uridyl.
5. A combinatorial library as claimed in ~~any one of the preceding claims~~ *claim 1* wherein the cap monomer is methyl (Me), formyl (CHO), ethyl (Et), acetyl (Ac), t-butyl (t-bu), anisyl, trifluoroacetyl (Tfa), benzoyl (Bz), 4-methylbenzyl (Meb), thioanisyl, thiocresyl, benzyloxymethyl, 4-nitrophenyl (Pnp), benzyloxycarbonyl (Z), 2-nitrobenzoyl (NBz), 2-nitrophenylsulphenyl (Nps), 4-toluenesulphonyl (Tosyl, Tos), pentafluorophenyl (Pfp), diphenylmethyl (Dpm), 2-chlorobenzyloxycarbonyl (Cl-Z), 2,4,5-trichlorophenyl, 2-bromobenzyloxycarbonyl (Br-Z), triphenylmethyl (Trityl, Trt), 2,2,5,7,8-pentamethyl-chroman-6-sulphonyl (Pmc), t-butylloxycarbonyl (Boc), benzyl (Bzl), benzyloxymethyl (Bom), and 9-fluorenylmethyloxycarbonyl (Fmoc).
6. A combinatorial library as claimed in ~~any one of the preceding claims~~ *claim 1* wherein the spacer monomer is a single amide linked amino acid, an amide linked dipeptide, or an amide linked tripeptide, or a mimetic thereof.
7. A nucleoside peptide molecule comprising a nucleoside monomer; a spacer monomer coupled to a nucleoside monomer, wherein the spacer monomer comprises one or more amide linked amino acid residues, or a mimetic thereof; and cap monomers attached to the spacer monomer.
8. A nucleoside peptide molecule of the formula I:



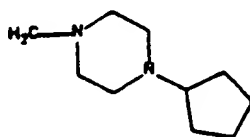
where X is H, -COOH, -OSO<sub>3</sub>H, or (CH<sub>2</sub>)<sub>q</sub>SO<sub>3</sub>H where q is 0 or 1, and R represents (Y)<sub>m</sub> where Y is an amide linked amino acid residue and m is 1-3, Z' and Z are the same or different and represent hydroxyl or alkoxy, or Z' and Z together form an acetonide group, and wherein free NH<sub>2</sub> groups in the compound of the formula I are capped with a cap monomer.

9. A nucleoside peptide molecule of the formula I as claimed in claim 8 wherein X is H, -COOH, -OSO<sub>3</sub>H, or (CH<sub>2</sub>)<sub>q</sub>SO<sub>3</sub>H where q is 0 or 1, Z and Z' are both hydroxyl or together form an acetonide group. R represents -NHCOR<sup>1</sup>, wherein R<sup>1</sup> represents

10 (a)  $-\text{C}(\text{CH}_3)(\text{NH}_2)\text{CH}_2-\text{C}_6\text{H}_4-\text{R}^2$ , wherein R<sup>2</sup> is alkoxy; or

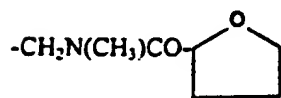
(b)  $-\text{CHR}^3\text{R}^4$  wherein R<sup>3</sup> is hydrogen or -NH<sub>2</sub> and R<sup>4</sup> is  $\text{C}_6\text{H}_4-\text{R}^5$  wherein R<sup>5</sup> is

15 halogen, alkyl, or alkoxy,



,  $-\text{CH}_2\text{N}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{R}^6$  or  $-\text{N}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{R}^6$

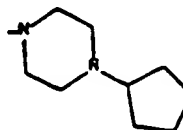
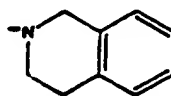
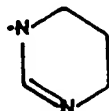
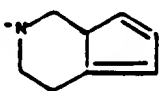
wherein R<sup>6</sup> is halogen,



,  $-\text{CH}_2\text{N}(\text{C}_2\text{H}_5)\text{CH}_2\text{CH}(\text{CH}_3)\text{OH}$ , or  $-\text{CH}_2\text{NHCOCH}(\text{CH}_3)_2$ , or

R<sup>4</sup> represents (CH<sub>2</sub>)<sub>n</sub>R<sup>8</sup> wherein n = 0 to 5, R<sup>8</sup> is halogen,  $\text{C}_6\text{H}_4-\text{R}^9$  wherein R<sup>9</sup> is

25 alkoxy,



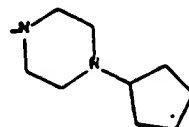
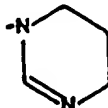
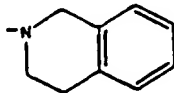
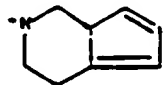
$-\text{N}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{R}^{10}$  wherein R<sup>10</sup> is halogen,  $-\text{N}(\text{C}_2\text{H}_5)\text{CH}_2\text{CH}(\text{CH}_3)\text{OH}$ , or  $-\text{NHCOCH}(\text{CH}_3)_2$  and wherein free amino groups are protected with a cap monomer.

30 10. A nucleoside peptide molecule of the formula I as claimed in claim 8 wherein X is -COOH, and R represents -NHCOR<sup>1</sup> wherein R<sup>1</sup> represents  $-\text{CHR}^3\text{R}^4$  wherein R<sup>3</sup> is hydrogen, and R<sup>4</sup> is (CH<sub>2</sub>)<sub>n</sub>R<sup>8</sup>

wherein n = 0 to 5, preferably 1 to 4, R<sup>8</sup> is halogen, alkyl,




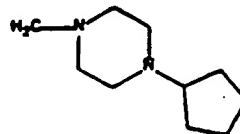
$\text{C}_6\text{H}_4-\text{R}^9$  wherein R<sup>9</sup> is alkoxy, halogen, or alkyl,



35  $-\text{N}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{R}^{10}$  wherein R<sup>10</sup> is halogen,  $-\text{N}(\text{C}_2\text{H}_5)\text{CH}_2\text{CH}(\text{CH}_3)\text{OH}$ , or  $-\text{NHCOCH}(\text{CH}_3)_2$ .

11. A nucleoside peptide molecule of the formula I as claimed in claim 8 wherein X is  $-\text{COOH}$ , and R represents  $-\text{NHCOR}^1$  wherein  $\text{R}^1$  represents  $-\text{CHR}^3\text{R}^4$  wherein  $\text{R}^3$  represents  $-\text{NH}_2$  and  $\text{R}^4$


is   $-\text{R}^3$  wherein  $\text{R}^3$  is halogen, alkyl or alkoxy,



$-\text{CH}_2\text{N}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{R}^6$  wherein  $\text{R}^6$  is halogen,  $-\text{CH}_2\text{N}(\text{C}_2\text{H}_5)\text{CH}_2\text{CH}(\text{CH}_3)\text{OH}$ ,  $-\text{CH}_2\text{NHCOCH}(\text{CH}_3)_2$

or  $-\text{CH}_2\text{N}(\text{CH}_3)\text{CO}-$  

12. A nucleoside peptide molecule of the formula I as claimed in claim 8 wherein X is  $-\text{OSO}_3\text{H}$ , or  $(\text{CH}_2)_q\text{SO}_3\text{H}$  where q is 0 or 1, R represents  $-\text{NHCOR}^1$  wherein  $\text{R}^1$  represents  $-\text{CHR}^3\text{R}^4$  wherein  $\text{R}^3$  represents  $-\text{NH}_2$  and  $\text{R}^4$  is

  $-\text{R}^3$  wherein  $\text{R}^3$  is halogen, alkyl, or alkoxy,  $-\text{CH}_2\text{N}(\text{C}_2\text{H}_5)\text{CH}_2\text{CH}(\text{CH}_3)\text{OH}$ , or  $-\text{CH}_2\text{NHCOCH}(\text{CH}_3)_2$ .

13. A process for preparing a combinatorial library containing a predetermined collection of nucleoside peptide molecules for inhibiting the transfer of a sugar from a selected sugar nucleotide donor having a heterocyclic amine base, to a selected acceptor by a carbohydrate processing enzyme comprising:

(a) coupling one or more amino acids, or mimetics thereof to a nucleoside monomer unit which comprises a heterocyclic amine base coupled to a sugar wherein the base corresponds to the heterocyclic amine base of the sugar nucleotide donor, or a modified form or analogue of the base; and

(b) capping any free functional groups or amine groups with a cap monomer unit.

14. A method of using a combinatorial library as claimed in claim 1 for screening for pharmacologically active molecules.

15. A solid-phase bioassay for identifying a compound having inhibitory activity against a carbohydrate processing enzyme which comprises (a) coupling an acceptor for the carbohydrate processing enzyme to a polymer and coating onto a carrier; (b) adding a carbohydrate processing enzyme, a sugar nucleotide donor labeled with a detectable substance, and a test compound; (c) measuring the detectable change produced by the detectable substance; and (d) comparing to a control in the absence of the test compound wherein a decrease in the amount of detectable substance with the test compound indicates that the test compound has inhibitory activity against the enzyme.

16. A method for identifying a compound that inhibits N-linked oligosaccharide processing comprising (a) reacting a test compound with cells expressing N-linked oligosaccharides in the presence of L-PHA and measuring alkaline phosphatase activity; and (b) comparing to a control in the absence of the compound wherein an increase in alkaline phosphatase activity indicates that the compound inhibits N-linked oligosaccharide processing.
- 5
17. A pharmaceutical composition containing a compound identified by a method as claimed in ~~any~~ <sup>claim 14</sup> one of claims 14, 15, or 16.

add A1

006070 515 010900